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EXAMINER	
WHISENANT, ETHAN C	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,659	ZHANG ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL ACTION

1. **Claim(s) 1-22** as originally filed 14 MAR 01 is/are pending in this application.

SEQUENCE RULES

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

DRAWINGS

3. The drawing(s) filed 14 MAR 01 with this application have been approved by the Examiner under 37 CFR 1.84 or 1.152.

35 USC § 112- 2ND PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS UNDER 35 USC § 112- 2ND PARAGRAPH

5. **Claim(s) 1-22** is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because there is no nexus between the preamble and the claim steps. Claim 1 in its preamble direct to a method which is to accomplish a particular goal. However, none of the claim steps states that this goal is accomplished. For clarity, claimed methods should recite that the purpose of the method has been attained (i.e. provide a nexus between the preamble and the claim steps). Furthermore, as regards Claim 1 it is unclear as to the exact method being claimed. The preamble makes the claim confusing. In addition, Claim 1 is indefinite because the phrases " the labeled nucleotide from the extended products without labeled nucleotide and from non-extended primers" in step (c) and "the solid support" in step (d) lack proper antecedent basis. Finally, step (d) is redundant of step(c). One must necessarily detect the labeled primer extension product when one is distinguishing the labeled extension products from unlabeled extension products and from non-extended primers.
Please clarify.

Claims 5 and 6 are confusing and therefore indefinite because of the phrase "said primer is unmodified oligonucleotides" in Claim 5 and the phrase "said primer is modified oligonucleotides" in Claim 6. It is unclear what is intended. Please clarify.

Claim 7 is confusing and therefore indefinite because of the phrase "said primer is labeled at the 3' terminals. A primer will have a 3' terminal while primers will have 3' terminals. It is unclear what is intended. Please clarify.

Claim 8 is confusing and therefore indefinite because of the phrase "said primer is labeled more than one nucleotides. A primer is composed of nucleotides, one or more of which can be labeled. However, the phrasing used as recited above does not make clear what is intended. Please clarify.

Claim 17 is confusing because of the phrase "wherein said primer extension is performed with DNA polymerase including DNA dependent DNA polymerase and RNA dependent DNA polymerase." It is unclear to the examiner if the primer extension reaction is to be performed with both

DNA dependent DNA polymerase and RNA dependent DNA polymerase in the reaction mixture or if this claim simply recites an improper Markush group. The examiner believes that this claim recites an improper Markush group as there is no basis in the specification for a primer extension reaction performed with both DNA dependent DNA polymerase and RNA dependent DNA polymerase in the reaction mixture. Please clarify.

Claim 18 is indefinite because it is unclear what is meant by the phrase "unlabeled substrates of dNTPs." In the prior art rejection which follows this phrase has been interpreted as if the claim reads The method according to Claim 1 wherein said primer extension is performed using unlabeled dNTPs.

35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e).

8. The prior art rejection(s) which follow are made in view of the ambiguity of the claims and using the examiner's best interpretation of claims in light of the specification.

CLAIM REJECTIONS UNDER 35 USC § 102

9. **Claim(s) 1-4, 6-14, 16-19 and 22** is/are rejected under 35 U.S.C. 102(b) as being anticipated by Pastinen et al. (1997).

Claim 1 is drawn to a method of genetic analysis which method comprises four required steps. To begin, target specific primer sets are prepared. Next, primer extension is performed. Then, the extended products containing the labeled nucleotide are distinguished from extended products without labeled nucleotide and from non-extended primers. Finally, the labeled product from primer extension left on the solid support is detected.

Pastinen et al. teach to a method of genetic analysis which comprises the four required steps recited in Claim 1.

Claim 2 is drawn to a embodiment of the method of Claim 1 wherein the primer sets are paired primers. **Claim 3** is drawn to a embodiment of the method of Claim 1 wherein the primer sets are unpaired primers. Pastinen et al. teach using both paired and upaired primers. See at least for example, p.611-612 and note especially Table2 which shows the primer pairs used (i.e. the PCR primers) as well as the unpaired primers used (i.e. the minisequencing primers).

Claim 4 is drawn to a embodiment of the method of Claim 1 wherein the primer sets are are unlabeled.

Pastinen et al. teach using both paired and upaired primers. See at least for example, p.611-612 and note especially Table 2 which shows the primer pairs used (i.e. the PCR primers) as well as the unpaired primers used (i.e. the minisequencing primers). Pastinen et al. teach using both labeled and unlabled oligos. Note that the minisequencing primers are unlabeled prior to the primer extension method.

Claim 6 is drawn to a embodiment of the method of Claim 1 wherein the primer a modified oligonucleotide.

All of the primer sets, paired and upaired, taught by Pastinen et al. have been modified in some

way . See at least for example, Table 2 on p.612.

Claim 7 is drawn to a embodiment of the method of Claim 1 wherein the primer is labeled at the 3' terminals.

Pastinen et al. teach this limitation. See at least for example Figure 2.

Claim 8 is drawn to a embodiment of the method of Claim 1 wherein the primer said primer is labeled at more than one nucleotides.

Pastinen et al. teach this limitation. See at least for example Figure 2 and Table 2 on p.612. Note that the minisequencing primers are labeled at their 3' terminal with the labeled ddNTP incorporated during primer extension and at their 5' ternminals with a 5' amino group. Thus the primer (i.e. the minisequencing primers) of Pastinen et al. are labeled at more than one nucleotide.

Claim 9 is drawn to a embodiment of the method of Claim 1 wherein said target specific primers sets are primers consisting of different subset of primers with similar nucleotide sequences except at least having one mismatched nucleotide A, T, C, G respectively.

Pastinen et al. teach this limitation. See at least for example Table 2 on p.612. Note that the PCR primers in Table are target specific primers sets are primers consisting of different subset of primers with similar nucleotide sequences except at least having one mismatched nucleotide A, T, C, G respectively.

Claim 10 is drawn to a embodiment of the method of Claim 9 wherein said target specific primer sets are immobilized on a solid support before primer extension.

Pastinen et al. teach this limitation. See at least, for example p.607 Column 2, in the section entitled "Design of the array".

Claim 11 is drawn to a embodiment of the method of Claim 9 wherein said target specific primer sets are added into a liquid phase for primer extension.

Pastinen et al. teach this limitation. See at least for example p.611 in the section entitled "PCR".

Claim 12 is drawn to a embodiment of the method of Claim 10 wherein said primer extension is solid phase primer extension.

Pastinen et al. teach this limitation. See at least for example p.611 in the section entitled "Minisequencing reactions."

Claim 13 is drawn to a embodiment of the method of Claim 10 wherein said primer extension is cascade primer extension.

Pastinen et al. teach this limitation. See at least for example pp. 610-613 in the section entitled "Methods". Please note that the examiner has used the applicants definition for the phrase "cascade primer extension" (i.e. The sample to be analyzed is used as the template for liquid phase primer extension initially. The template for solid phase primer extension is mainly the product from the liquid phase primer extension.

Claim 14 is drawn to a embodiment of the method of Claim 10 wherein said primer extension is post-hybridization primer extension.

Pastinen et al. teach this limitation. See at least for example pp. 610-613 in the section entitled "Methods", note especially the section entitled "Minisequencing reactions", on pp. 611-612.

Claim 16 is drawn to a embodiment of the method of Claim 1 wherein said primer extension is performed at a temperature higher than 37°C.

Pastinen et al. teach this limitation. See, at least for example, pp. 610-613 in the section entitled "Methods", note especially the section entitled "Minisequencing reactions", on pp. 611-612.

Claim 17 is drawn to a embodiment of the method of Claim 1 wherein said primer extension is performed with a DNA polymerase which is selected from a defined group which consists of a DNA dependent DNA polmerase and a RNA dependent DNA polymerase.

Pastinen et al. teach this limitation. See at least for example pp. 611-613 in the section entitled "Minisequencing reactions". Please note the 112, 2nd paragraph rejection above against claim 17.

Claim 18 is drawn to a embodiment of the method of Claim 1 wherein said primer extension is performed using unlabeled dNTPs.

Pastinen et al. teach this limitation wherein these authors teach PCR. See at least for example pp. 611 in the section entitled "PCR". Please note the 112, 2nd paragraph rejection above against claim 18.

Claim 19 is drawn to a embodiment of the method of Claim 1 wherein said primer extension is performed using unlabeled dNTPs with labeled nucleotides.

Pastinen et al. teach this limitation wherein these authors teach PCR. See at least for example pp. 611 in the section entitled "PCR".

Claim 22 is drawn to a embodiment of the method of Claim 1 wherein said extended product containing labeled nucleotide is distinguished from the extended product without labeled nucleotide by visualization and detection.

Pastinen et al. teach this limitation wherein these authors teach PCR. See at least for example pp. 611-613 in the section entitled "Minisequencing reactions".

35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

12. **Claim(s) 5** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Pastinen et al. (1997) as applied to Claim 1 above and further in view of Goelet et al. [US 6,004,744 (1999)].

Claim 5 is drawn to a embodiment of the method of Claim 1 wherein said primer is unmodified oligonucleotides.

As discussed above, all of the oligos utilized by Pastien et al. were modified in some way. Therefore, it can be said that Pastien et al. teach all of the limitations of Claim 5 except these authors do not teach using a primer which is an unmodified oligonucleotide. However, as the use of primers which are unmodified was well known in the art at the time of the invention as evidenced by, at least for example, Goelet et al. See Figure 2, Panels I-III. In light of these findings and absent an unexpected

result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use unmodified oligonucleotide(s) in the method of Pastien et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

13. **Claim(s) 15** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Pastinen et al. (1997) as applied to Claim 1 above and further in view of Cohen et al. [US 5,525,470 (1996)].

Claim 15 is drawn to a embodiment of the method of Claim 1 wherein said primer extension is performed at 37°C.

Pastinen et al. teach all of the limitations of Claim 15 except these authors do not teach performing their primer extension reaction (i.e. the minisequencing reactions) at 37°C. Instead these authors teach using a number of different DNA polymerases used at temperatures from 50°C to 60°C. See at least for example, pp. 613 in the section entitled "Minisequencing Reactions". However, as the use of DNA polymerases which extend primers at 37°C (e.g. Sequenase 2.0) was well known in the art at the time of the invention as evidenced by, at least for example, Cohen et al. (see the para bridging Column 11-12), it would have been, absent an unexpected result, *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of method of Pastien et al. wherein the DNA polymerase utilized is Sequenase 2.0 (i.e. a DNA polymerase which extend primers at 37°C). Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

14. **Claim(s) 18-19** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Pastinen et al. (1997) as applied to Claim 1 above and further in view of Ugozzoli et al. [US 5,525,470 (1996)].

Claim 18 is drawn to a embodiment of the method of Claim 1 wherein said primer extension is performed using unlabeled dNTPs.

Pastinen et al. teach all of the limitations 18 except these authors do not teach performing their primer extensions (i.e. their minisequencing reactions) with unlabeled dNTPs, rather these author use label and unlabeled ddNTPs in their primer extensions (i.e. their minisequencing reactions). See at least for example pp. 611-613 in the section entitled "Minisequencing reactions". However, as the use of unlabeled dNTPs in primer extension type assays was well known in the art at the time of the invention as evidenced by Ugozzoli et al. -see at least for example, Figure 1 - it would have been, absent an unexpected result, *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of method of Pastien et al. wherein unlabeled dNTPs are used in the primer extension reactions (i.e. the minisequencing reactions). Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 19 is drawn to a embodiment of the method of Claim 1 wherein said primer extension is performed using unlabeled dNTPs with labeled nucleotides.

Pastinen et al. teach all of the limitations 19 except these authors do not teach performing their primer extensions (i.e. their minisequencing reactions) with unlabeled dNTPs, rather these author use label and unlabeled ddNTPs in their primer extensions (i.e. their minisequencing reactions). See at least for example pp. 611-613 in the section entitled "Minisequencing reactions". However, as the use of unlabeled dNTPs in primer extension type assays was well known in the art at the time of the invention as evidenced by Ugozzoli et al. -see at least for example, Figure 1 - it would have been, absent an unexpected result, *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of method of Pastien et al. wherein unlabeled dNTPs are used in the primer extension reactions (i.e. the minisequencing reactions). Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the

motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

CONCLUSION

15. **Claim(s) 1-22** is/are rejected and/or objected to for the reason(s) set forth above.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

The fax number for this Examiner is (571) 273-0754. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

ETHAN WHISENANT
PRIMARY EXAMINER

Art Unit 1634